

COMPARATIVE STUDY OF NEUTROPHIL LYMPHOCYTE RATIO (NLR) IN PULMONARY TUBERCULOSIS PATIENTS WITH AND WITHOUT DIABETES MELLITUS

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ABSTRACT

Background: Tuberculosis (TB) lungs is disease infection which caused by *Mycobacterium Tuberculosis* (M.TB) bacteria. The risk of pulmonary TB can increase in people with diabetes mellitus (DM). The occurrence of infection is closely related to response immune. Pulmonary TB infection causes inflammation resulting in changes in the immune system in the form of an increase in the number of neutrophils (neutrophilia) and a decrease in the number of lymphocytes (lymphocytopenia). Chronic inflammation is also experienced by DM sufferers due to hyperglycemia which damages the endothelium and triggers a cellular response resulting in an increase in NLR. This study aims to determine the overview of NLR in pulmonary TB patients with DM.

Method: This type of research is descriptive research with a *cross sectional approach*. This research uses a *convenience sampling technique*. This research was conducted in month April-June 2024 with A sample of 40 TB patients without DM and TB patients with DM from several health centers center in Jambi City.

Result: The result shows the average number of NLR in pulmonary TB without DM which is 1,60 and in pulmonary TB with DM the average was 2,59. Results of *Mann Whitney test* with mark p-value = 0.006 (p<0.05)

Conclusion: NLR in pulmonary TB with DM is higher than NLR in pulmonary TB without DM.

Keywords: pulmonary TB without DM, Pulmonary TB with DM, NLR

INTRODUCTION

Pulmonary tuberculosis (pulmonary TB) is a lung infection caused by the bacteria *Mycobacterium Tuberculosis* (M.TB) and is still a health problem throughout the world. Pulmonary TB is the main cause of death due to infectious diseases with high morbidity and mortality rates. Based on data from *the World Health Organization* (WHO), pulmonary TB cases are often found in developing countries with low and middle income. Some of them are India, Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh and the Democratic Republic of the Congo (WHO, 2022).

WHO report In 2022, it is estimated that there will be 10.6 million cases of pulmonary TB with a death rate of 1.3 million people in the world (WHO, 2022). Indonesia is ranked second as a contributor to pulmonary

TB morbidity after India with 969,000 sufferers (Kemenkes RI, 2022). The Central Statistics Agency (BPS) reported that in Jambi Province, 12,682 people were found suffering from pulmonary TB and 1,942 of them were in Jambi City (BPS, 2022).

The risk of pulmonary TB can increase in people with diabetes mellitus (DM), in fact, according to WHO, in 2019 it is estimated that there will be 0.35 million cases of TB lungs caused by DM (WHO, 2022). The Jambi City Health Service recorded that in 2022 there were 91 pulmonary TB patients with DM (Dinkes, 2022). Research conducted by Arliny (2015) shows that DM is an important risk factor for pulmonary TB and can influence clinical and treatment response, and even increase the risk of developing drug-resistant pulmonary TB (MDR TB).

DM patients have a low immune system which can trigger an increase in latent

pulmonary TB to active pulmonary TB. DM also has a negative impact on the results of pulmonary TB treatment because it causes a delay in the microbiological response and a higher initial burden of mycobacterial numbers as well as a longer sputum conversion time, causing a higher recurrence rate. DM sufferers may also be at risk of failure in pulmonary TB therapy compared to patients who do not suffer from DM. On the other hand, pulmonary TB infection can also cause glucose intolerance, triggering hyperglycemia which will worsen glycemic control and can result in DM in susceptible people (Arliny, 2015; Lin et al., 2019; Mihadja et al., 2016).

According to Lin et al. (2019) an increased risk of pulmonary TB occurs in both type 1 and type 2 DM, however type 2 DM accounts for more than 95% of patients worldwide so that the public health burden due to comorbid diseases from type 2 DM is much greater. This is in accordance with the research results of Utomo et al. (2016) which shows that there is a significant relationship between type 2 DM and extensive pulmonary TB lesions ($p=0.03$). Type 2 DM is known to increase the risk of pulmonary TB lesion status by 5.25 times.

Pulmonary TB infection causes inflammation resulting in changes in the immune system in the form of an increase in the number of neutrophils (neutrophilia) and a decrease in the number of lymphocytes (lymphocytopenia). The results of the comparison between neutrophils and lymphocytes are more sensitive in the incidence of bacterial infections when compared with the total white blood cell count. The comparison of the number of neutrophils and lymphocytes, which has become known as the *Neutrophil Lymphocyte Ratio* (NLR), has become a new marker of inflammation that has the potential to determine the presence of chronic inflammation which can be detected simply, efficiently and reliably because of its stability and high sensitivity. Chronic inflammation is also

experienced by DM patients due to hyperglycemia which will damage the endothelium (endothelial dysfunction) and trigger a cellular response resulting in an increase in NLR (American Diabetes Association, 2015; Azab et al., 2014; Y.-H. Lin et al., 2015; Nurdin et al., 2021).

Research conducted by Ngahane et al., (2020) stated that there was a significant increase in NLR in pulmonary TB patients compared to the control group. This is in line with research by Jeon et al., (2019) which obtained an average NLR value in the pulmonary TB group, which was 4.37, higher than the healthy group. NLR was also significantly higher in Type 2 DM patients who experienced complications. In research conducted by Nurdin et al., (2021), the results of NLR examinations in Type 2 DM sufferers were obtained, namely that 26 samples (86.67%) had increased NLR and four samples (13.33%) had normal NLR.

The research data above shows an increase in NLR experienced by pulmonary TB patients and DM patients due to the body's response to inflammation. This is what underlies the author's interest in conducting research to try to see the picture of NLR in pulmonary TB patients suffering from DM.

METHODS

This research is a study with a cross-sectional design. Sampling using convenience sampling techniques was carried out on pulmonary TB patients at several Community Health Centers in Jambi City. The number of samples in this study was 40 samples consisting of 20 pulmonary TB patients without DM and 20 pulmonary TB patients suffering from DM who were undergoing treatment at 9 health centers in Jambi City (Payo Selincah, Kenali Besar, Talang Bakung, Talang Banjar, Tanjung Pinang, Simpang Kawat, Paal Merah I, Paal V and Pakuan Baru).

The patient filled out and signed a consent form as a research respondent before the interview. Next, a sample of the patient's venous blood is taken. The specimen is examined using a Hematology Analyzer (Sysmex XN-450). Statistical data were analyzed using the Mann Whitney test using the statistical program for social science (SPSS.23).

RESULTS AND DISCUSSION

In this study, observations were made on examination data from 20 pulmonary TB patient without DM and 20 pulmonary TB patient with DM respondents.

3.1 General characteristics of research Subjects
The characteristics of the respondents involved can be seen below:

Table 1. Respondent characteristic table

Characteristics	Pulmonary TB without DM		Pulmonary TB with DM	
	N	%	N	%
Gender				
▪ Man	10	50%	10	50%
▪ Woman	10	50%	10	50%
Age				
▪ 15 – 64	19	95%	17	85%
▪ ≥ 65	1	5%	3	15%
Length of treatment for TB				
▪ ≤ 2 months	8	40%	10	50%
▪ > 2 months	12	60%	10	50%
Duration of Suffering for DM				
▪ < 5 years	-	-	9	45%
▪ > 5 years	-	-	11	55%

Analysis characteristics of respondents in pulmonary TB patients without DM and pulmonary TB with DM, namely gender, both have the same percentage, namely men (50%) and women (50%). Based on age, respondents with pulmonary TB without DM and pulmonary TB with DM were dominated by the age group 15-64 years old. Analysis of the length of treatment in TB patients showed respondents with treatment duration >2 months more (60%) than respondents with duration of treatment ≤ 2 months (40%), while in TB patients with DM respondents had the same percentage with duration of treatment ≤ 2

months (50%) and > 2 months (50%). Based on the length of DM treatment, TB patients with DM were dominated by treatment duration >5 years (55%).

3.2 Description of NLR in patients Pulmonary TB with and without DM

Table 2. Neutrophils to lymphocyte ratio based on respondent

Variable	N	Mean	Std. Deviation	P value
TB without DM	20	1,60	0,95	
TB with DM	20	2,59	1,51	0.006

Based on the table above, it can be seen that pulmonary TB patients suffering from DM have the highest average NLR (2.59). The results were analyzed using the *Mann Whitney test* and obtained a p value = 0.006. The *p value* is smaller than *alpha* (α) 0.05, so it can be concluded that there is a significant difference between the average NLR in pulmonary TB patients suffering from DM and without DM as indicated by the higher NLR in pulmonary TB patients suffering from DM.

Pulmonary TB infection causes inflammation resulting in changes in the immune system in the form of an increase in the number of neutrophils (neutrophilia) and a decrease in the number of lymphocytes (lymphocytopenia). The results of the comparison between neutrophils and lymphocytes are more sensitive in the incidence of bacterial infections when compared with the total white blood cell count. (Azab et al., 2014; Y.-H. Lin et al., 2015; Nurdin et al., 2021).

The relationship between NLR and infection also exists in chronic inflammation suffered by DM patients. Hyperglycemia results in impaired neutrophil function so that comotactic, phagocytic and bacterial killing power decreases. DM is associated with decreased cellular immunity, T lymphocytes and neutrophils, decreased T-helper1 (Th1) cytokine response, TNF alpha production, IL-1 beta and IL-6 production found in TB-DM compared to non-DM. Th1 cytokines are vital in controlling and inhibiting M.TB. The

decrease in the number and function of T lymphocytes causes the susceptibility of DM to develop into TB (Santos et al., 2018; Woelansari et al., 2024).

The results of research conducted on the average NLR based on respondent status showed that the average NLR in pulmonary TB patients with DM was 2.59, higher than the average NLR in pulmonary TB patients without DM, which was 1.60. These results are in line with research conducted by Dewi et al., (2018) which stated that the NLR in TB patients was known to be higher in patients with poor glycemic control. This condition can occur because NLR is related to glycemic control and pulmonary TB infection, so it has an impact on cell increased neutrophils (neutrophilia) And cell lymphocytes decrease (lymphocytopenia) (American Diabetes Association, 2015; Azab et al., 2014; Dewi et al., 2018; Y.-H. Lin et al., 2015; Nurdin et al., 2021).

TB patients with DM experience high levels of depression of cellular immunity, with the presence of fewer T lymphocytes and decreased capacity compared to patients with TB alone. DM causes a decrease in the phagocytic power of macrophages, which can affect the body's defences. This is supported by the observation that uncontrolled DM sufferers can experience a more destructive increase in TB and a higher death rate. (Faurholt-Jepsen et al., 2011; Niazi et al., 2012).

Higher NLR is a potential marker of inflammation and can lead to the severity of TB disease, insulin resistance and type 2 diabetes. Hyperglycemia was found to be associated with suppression of innate and adaptive immune responses in TB-DM patients due to the absolute number of total T and B lymphocytes, CD8⁺ T lymphocytes, and NK cells were found to be lower. Higher levels of pro-inflammatory cytokines were observed in TB-DM patients compared with non-DM patients before and during anti-tuberculosis

therapy (Abakay et al., 2015; Lou et al., 2015; Prada-Medina et al., 2017)

Mann Whitney test carried out, it showed that there was a significant difference and obtained a p value = 0.006. The p value is smaller than alpha (α) 0.05, so it can be concluded that there is a significant difference between the average NLR in pulmonary TB patients suffering from DM and those without DM as indicated by the higher NLR in pulmonary TB patients suffering from DM. These results are in line with research conducted by Woelansari et al., (2024) stating that there is a relationship between NLR values in TB DM patients.

CONCLUSION

The results of research that has been carried out regarding NLR examination in pulmonary TB patients between those without DM and those with DM, it was found that the average NLR in pulmonary TB patients without DM was 1.60 and the average NLR in pulmonary TB patients with DM was 2.59. It can be concluded that there is a significant difference between NLR in pulmonary TB patients with DM and without DM. Future researchers are advised to continue research by examining other types of leukocyte cells and covering a wider research area so that they can describe the population evenly.

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CONFLICT OF INTEREST

There is no potential conflict of interest in this research.

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